

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

CLAIMS STATUS

Applicants have canceled claims 4, 6-7 and 9 without prejudice or disclaimer in order to advance the prosecution. Applicants reserve the right to file one or more new applications claiming canceled subject matter.

Applicants have amended claims 8, 11-13, 15-16, 18-19, 22-26, 29-30, 32-34 and 38-39. The amendment should be entered, because it cancels claims and/or presents the rejected claims in better form for consideration on appeal.

After the amendment, claims 8, 11-13, 15-16, 18-19, 22-26, 29-30, 32-34 and 38-39 are pending.

REJECTION UNDER 35 U.S.C. § 103(a)

Claims 4, 6, 8, 11-13, 15-16, 18-19, 22-26, 29-30, 32-34 and 32-39 stand rejected as obvious over SmithKline Beecham Co. (WO 95/06410) in view of Katz et. al. (US 5,028,435). Applicants traverse the rejection.

In particular, Applicants note that

(1) neither of the cited references teaches a skin permeability regulator comprising (A) a fatty acid ester, (B) a polyol and (C) a nonionic surfactant; and

(2) based on the teaching of cited documents, one of ordinary skill in the art would not have had the required motivation or the required reasonable expectation of success to combine a particular compound having angiotensin II antagonistic activity, 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate, and a particular skin permeability regulator comprising a fatty acid ester, a polyol and a nonionic surfactant.

With respect to point (1), the PTO expressly admitted that neither of the cited references discloses “the use of more than one permeability enhancer” (Office Action, page 2). Although the PTO states that “one of ordinary skill in the art would have the prerequisite knowledge to add additional enhancers to the formulation with a reasonable expectation of assisting the drug to permeate across the skin” (Office Action, page 2), the PTO fails to provide any evidence of “the prerequisite knowledge.” Applicants respectfully request the PTO to present such evidence, as without it, Applicants are in a difficult position of not being able to understand or rebut the PTO’s statement.

Even if such evidence were provided, one of ordinary skill in the art would lack the required motivation and the required expectation of success to combine in a percutaneous composition a particular compound having angiotensin II antagonistic activity, 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2’-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate, recited in claim 8, and a particular skin permeability regulator comprising a fatty acid ester, a polyol and a nonionic surfactant as Katz teaches that not every compound listed in the paragraph bridging columns 5 and 6 is as a permeability enhancer for every drug.

To support this point, Applicants refer to Katz, column 6, lines 3-9, that states: “the selection of drug, matrix layer, and chemical penetration enhancer cannot be made independently. Rather, the nature of the drug and the enhancer are **interdependent** as the enhancer **must be selected** to provide for transport of that drug across the skin or membrane of the host”. Katz’s statement that “the enhancer must be **selected**” clearly indicates that not every compound listed in the paragraph bridging columns 5 and 6 will act as permeability enhancer for every drug.

Applicants further note that Katz does not provide any specific criteria for selecting a particular permeability enhancer for any particular drug, nor does Katz teach any particular permeability enhancer or a combination of enhancers compatible with any compound having angiotensin II antagonistic activity, such as 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2’-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate recited in claim 8. Thus, one of ordinary skill in the art could only arrive to a combination of 1-

(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate and a particular skin permeability regulator comprising a fatty acid ester, a polyol and a nonionic surfactant in a percutaneous preparation by chance, i.e. quite opposite of the required motivation and required expectation of success.

Along these lines, Applicants respectfully note that the experimental examples of the instant application demonstrate that the skin permeability regulator comprising a fatty acid ester, a polyol and a nonionic surfactant successfully transports 1-

(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate through the skin, see Examples 1-3 and Test Example.

In conclusion, Applicants respectfully request withdrawal of the rejection for the following two reasons:

(1) neither Katz, nor the '410 publication teaches a skin permeability regulator comprising (A) a fatty acid ester, (B) a polyol and (C) a nonionic surfactant; and

(2) based on the teaching of Katz and the '410 publication, one of ordinary skill in the art would not have had the required motivation or the required reasonable expectation of success to combine a particular compound having angiotensin II antagonistic activity, 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate, and a particular skin permeability regulator comprising a fatty acid ester, a polyol and a nonionic surfactant.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment,

to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date Jan. 17, 2006

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